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SERUM GLUTAMIC OXALOACETIC TRANSAMINASE ACTIVITY AS AN INDEX OF ACUTE MYOCARDIAL DAMAGE*

Glutamic oxaloacetic transaminase (GO-T) is a specific tissue enzyme concerned with the transfer of the α-amino nitrogen of aspartic acid to α-ketoglutaric acid resulting in the synthesis of a new amino acid, glutamic acid, and a new α-keto acid, oxaloacetic acid. GO-T is widely distributed in animal and human tissues and its concentration or activity is greatest in heart muscle, skeletal muscle, brain, liver and kidney in decreasing order[1,2,3]. These facts suggested a study of its activity in sera following experimental and clinical myocardial damage[4,5,6,7].

Glutamic oxaloacetic transaminase activity has been demonstrated in all human and animal sera tested and appears to be species specific[8]. SGO-T (serum glutamic oxaloacetic transaminase) can be measured by paper chromatography[9], spectrophotometrically[9,10], and colorimetrically[11]. Although each method has its advantages and disadvantages, the technique which is most rapid and sensitive is the one used in our laboratory[9]. A unit of activity is arbitrarily defined as a decrease in optical density of 0.001 mu/ml/minute. The normal range in human sera is 22.1 units /ml/minute ± 6.8 units.

The enzyme is stable in serum for 4 days at refrigerator temperatures and loses little activity if stored at these temperatures up to 30 days. The plasma and serum levels are the same, are reproducible from day to day in the same normal individuals, and are unaffected by freezing or lyophilization. Heating to 100°C will destroy SGO-T activity. The ratio of the activity in normal dog and human serum to that of dog or human heart muscle is approximately 1:10,000[7].

Myocardial damage results in a decrease of GO-T activity in the injured heart muscle and is associated with an increase in the activity of the serum[7]. Increased SGO-T activity will develop following injury of heart muscle, skeletal muscle, liver and possibly kidney from circulatory, infectious, toxic or traumatic damage. Central nervous system injury is not associated with increases in SGO-T activity. The serum transaminase levels rise precipitously after death, and are highest in venous reservoirs draining tissues of maximal SGO-T activity[4].

Acute liver cell injury due to CCl_4 poisoning, infectious hepatitis or homologous serum hepatitis results in striking elevation of the SGO-T activity which is usually many times that seen following myocardial infarction or obstructive jaundice. Cirrhosis of the liver or metastases to the liver may be associated with normal, slight or moderate elevations of SGO-T[12]. Because of the clinical differences between liver disease and myocardial infarction as well as the difference in the serial alterations of transaminase levels, there is rarely any confusion between the two diagnoses on the basis of the SGO-T activity.

SGO-T activity has not been found to be increased in infectious, degenerative, neoplastic, allergic, reactive or congenital disease states, *unless* these are associated with acute damage to heart, skeletal muscle, liver or possibly kidney. No changes have been noted during the course of pregnancy or delivery. There is no constant relationship between the SGO-T activity and the erythrocyte sedimentation rate, the white blood count or the C-reactive protein levels.

EXPERIMENTAL STUDIES

Myocardial infarction was experimentally induced in dogs by the injection of plastic spheres into the coronary sinus. In every experiment the SGO-T activity increased, with peak levels appearing 9 to 23 hours post-infarction, sometimes reaching values 20 to 30 times that of the control level. It was found that there was a relatively linear correlation between the amount of infarction estimated at autopsy and the maximal rise in SGO-T activity (peak level). The animals with the highest SGO-T levels had the greatest degree of myocardial infarction. The SGO-T rise following myocardial necrosis resulting from the intravenous injection of papain into rabbits resulted in peak levels in individual experiments that were again roughly proportional to the degree of necrosis found at autopsy[13].

Myocardial infarction was again produced in dogs by tightening a ligature ten days after it had been placed about a coronary artery. In each of

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fifteen infarcts caused in this manner the SGO-T activity increased and it was again demonstrated that the higher the SGO-T activity, the larger the infarct. A 0.5 gram infarct resulted in a peak SGO-T of 64 units (20 above normal) and an 18 gram infarct resulted in levels up to 500 units. The duration of abnormally increased but falling SGO-T activity was 4-5 days in animals with larger infarcts, and 24 hours in the case of smaller areas of infarction. Thus, both the height and duration of increased enzyme activity appeared to be proportional to the size of the infarct. In this study analysis of the homogenates of the infarcted heart muscle showed a progressive decrease in GO-T activity, proportional to the age of the infarct[7]. Uninfarcted muscle from the same animal showed normal concentrations of GO-T.

Myocardial ischemia in dogs was produced by lifting a sling placed 10 days previously under a coronary artery so as to cause T wave and ST segment changes but no Q wave changes. Four of these animals developed myocardial infarction and all had elevated SGO-T activity. In the remaining 11, the SGO-activity remained within normal limits in all but one, despite the appearance of temporary electrocardiographic evidence of ischemia manifested by ST segment and T wave changes.

CLINICAL APPLICATIONS

Myocardial Infarction

Sera obtained from 300 patients within 48 hours after the onset of unequivocal acute myocardial infarction and daily thereafter have been analyzed for SGO-T activity. In all but three instances when the serum was obtained at the time of acute infarction, the SGO-T activity rose two to twenty times the normal within the first 48 hours (Figure 1). The height and duration of increased SGO-T activity appeared to be roughly proportional to the size of the infarct as estimated electrocardiographically[4]. Secondary elevations of SGO-T were noted following recurrent chest pain associated with the extension of the original area of infarction or the occurrence of a new infarction in the same patient.

In some instances when left bundle branch block obscured the diagnostic electrocardiographic evidence of infarction, the SGO-T showed clear-cut evidence of myocardial necrosis. In other instances no elevation was observed, which suggested the absence of infarction. The clinical course of this group of patients usually indicated that infarction was present when the transaminase was elevated. Four patients were studied who demonstrated electrocardiographic evidence suggestive of subendocardial infarction. In two, clear-cut increases in SGO-T activity occurred. The electrocardiographic abnormalities in the other two patients reverted toward normal when digitalis was withdrawn. When SGO-T was elevated in patients who exhibited equivocal electrocardiographic changes, the usual treatment for myocardial infarction was instituted. However, if the transaminase level was normal, patients were

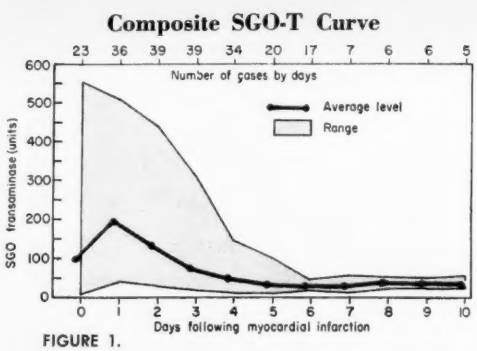

FIGURE 1.

usually allowed out of bed within one week. These findings have been corroborated elsewhere[14].

No correlation has been found between the SGO-T activity and the white blood count, the sedimentation rate, the presence or absence of shock, the absolute levels of the blood pressure, the presence of heart failure, the location of the infarction, the mortality rate, or the use of anticoagulant drugs. There was a significant correlation, however, between the SGO-T activity and the electrocardiographically estimated size of the infarct. The higher enzyme levels were associated with more extensive electrocardiographic changes.

Angina Pectoris and Coronary Insufficiency

SGO-T activity has not been found to be increased in patients with simple angina pectoris. Fifty patients who had coronary insufficiency showed electrocardiographic changes of ischemia and these changes consisted of moderate to marked T wave inversion, sometimes associated with ST segment changes, but without Q wave abnormalities. Thirty-four patients had normal SGO-T activity even though they had experienced persistent substernal chest pain for a long time. Sixteen had elevated serum enzymatic activity compatible with acute muscle cell damage. It is interesting that of these 16 patients, 8 developed SGO-T elevation at least three days after the onset of their chest pain[16].

Pericarditis

Eleven patients with unequivocal evidence of pericarditis were studied. Two showed minor elevations of SGO-T which may have been due to the presence of co-existent liver disease. The remaining 9 patients showed no alterations in SGO-T activity during the acute phase of their disease[16].

Rheumatic Carditis

Preliminary studies of SGO-T levels during rheumatic fever have shown increased activity in approximately 50% of the patients with clinical or histologic evidence of active rheumatic carditis. Normal levels were seen in all but one of the patients who had rheumatic fever without definite evidence of carditis. Some patients with

active carditis, however, had normal SGO-T activity[17].

Pulmonary Infarction

The SGO-T activity was followed during the course of pulmonary infarction in 7 patients. Normal levels were obtained in 6 patients, and the seventh patient showed a peak enzyme activity of 50 units[17].

DISCUSSION

The spectrophotometric technic is the most accurate and rapid procedure for the SGO-T determination. We have used the Beckman DU instrument for our spectrophotometric determinations. This method has been modified by Steinberg so that the Bausch and Lomb spectrophotometer may be used. This modification is recommended for smaller laboratories[10]. The colorimetric procedure, adapted from Umbreit, may prove widely useful[11]. Serum must be separated from red blood cells as soon as possible and stored at refrigerator temperatures not longer than 4 days. Finally, *unless serum is obtained from the patient within three days after the onset of infarction, the SGO-T activity cannot be relied upon as evidence of acute myocardial damage.*

Experimental and clinical myocardial infarction is followed by a characteristic SGO-T curve with the peak occurring within 24 hours and the activity falling to normal within two to five days (Figure 1). The height and duration of elevated enzyme activity is roughly proportional to the extent of myocardial necrosis. This determination, then, has particular significance in deciding whether acute heart muscle cell damage has occurred when chest pain, suggestive of acute myocardial infarction, appears and is associated with equivocal electrocardiographic changes, and other indefinite laboratory findings. Under these circumstances, if the analysis is done with the precautions described, many patients who have a normal SGO-T may be saved weeks of invalidism or unnecessary anticoagulant therapy. Conversely, in this group of patients, acute damage of heart muscle may be presumed to be present if there is an elevation of the SGO-T in the absence of known active liver disease.

Pericarditis and pulmonary infarction can be distinguished from acute myocardial infarction because the SGO-T is rarely and only slightly elevated in the former and usually remains within normal limits in the latter. Further study is needed to evaluate the changes of SGO-T activity in rheumatic carditis.

Infarcted heart muscle has been found to contain as little as one fiftieth the GO-T activity of normal heart muscle. This suggests that the increased serum levels following myocardial infarction are due to the release of this enzyme from damaged heart muscle cells in an amount in excess of that which the body can destroy or excrete. Other serum enzymatic activities have been found to rise after acute heart muscle cell damage. This is at present under study in our laboratory[18]. Deviations in various enzyme levels following tissue damage are not solely explicable on the basis of a simple release into the blood stream; other mechanisms as yet unknown remain to be elucidated.

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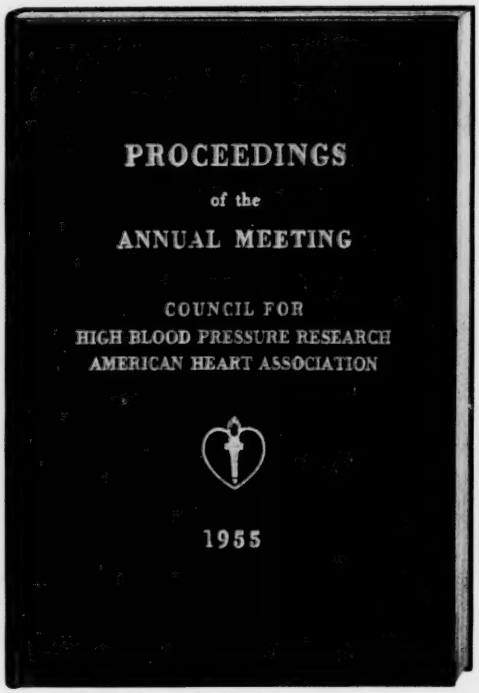

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The 29th Annual Scientific Sessions of the American Heart Association will be held in Cincinnati, Ohio, October 27, 28, 29, 1956 in conjunction with the Association's Annual Meeting. The deadline for submission of abstracts has been extended to June 15. Abstracts will be accepted only on forms which may be obtained from the Medical Director, American Heart Association, 44 East 23rd Street, New York 10, New York.

Papers intended for presentation should be based on original investigations in or related to the cardiovascular field. The abstracts must be 300 words or less and should contain in summary form the results obtained and the conclusions reached. Abstracts must be submitted in triplicate.

The Scientific Sessions this year will feature an enlarged section for Scientific Exhibits. Requests for space and application forms can also be obtained from the Association's Medical Director. The deadline for these applications has been extended to June 15, 1956. All exhibit applications will be acted upon by the Program Committee of the Scientific Council.